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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/087,513	KANEKO ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,15,19 and 21-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14 15 19 21-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 14, 15, 19 and 21-36 remain pending and are under consideration in the instant office action.

Applicant's arguments filed 8-12-04 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The rejection of claims 21, 24 and 26-36 under 35 U.S.C. 112, first paragraph, new matter, has been withdrawn in view of applicants' arguments. Specifically, the rejection regarding the phrase "deletion of amino acids 297-329 in said variable loop" as being new matter (claims 21, 24, 26, 27, 30 and 34) has been withdrawn. One of skill would have recognized that "Δ297-329" in the phrase "[t]he vv- ΔV3 mutant with the Δ297-329 deletion" referred to a deletion of amino acids 297-329 because the art at the time of filing described the V3 loop as being around amino acids 300-321 (BH10 strain) and may vary slightly from strain to strain (see ¶ 18 of Declaration by Danuta Kozbor filed 8-12-04).

I. Claims 14, 15, 19 and 21-36 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record.

The claims require DNA encoding an envelope glycoprotein of HIV having a deletion of the third variable loop. The specification discloses the WTP-2, WTP-5 and WTP-8 (pg 35, line 3; pg 36, line 16; Fig. 1) but does not teach they have a deletion of the V3 loop as claimed or provide the structure of the vectors. The only DNA encoding an envelope glycoprotein of HIV having a deletion of the V3 loop described in the specification are vv-ΔV3 (pg 26, line 16) and 1ΔV3, 7ΔV3 and 8ΔV3 (pg 34). However, the specification does not provide adequate written description for one of skill to make vv-ΔV3 (pg 26, line 16), 1ΔV3, 7ΔV3 or 8ΔV3. Therefore, the specification does not provide adequate written description for DNA encoding an envelope glycoprotein of HIV having a deletion of the V3 loop as claimed.

The specification does not provide adequate written description for vv-ΔV3. Kmieciak (June 1, 1998, J. Immunol., Vol. 160, pg 5676-5683) teaches vv-ΔV3 was made using "the Δ297-329 deletion" taught by Wyatt (Dec. 1992, J. Virology, Vol. 66, pg 6997-7004). The Δ297-329 deletion of Wyatt was a deletion spanning amino acids 297-329 of the V3 loop and an insertion of Gly-Ala-Gly in place of the loop. The specification does not teach, suggest or hint that Gly-Ala-Gly was inserted into the Δ297-329 deletion as taught by Kmieciak in view of Wyatt. Nor was Kmieciak available to one of skill at the time the application was filed (5-29-98). One of skill would have had no way of knowing that the "Δ297-329 deletion" described in the specification was the mutation described by Wyatt and that the mutation also included inserting Gly-Ala-

Gly into the Δ297-329 deletion. Without such description, the specification does not adequately describe the structure of the vv-ΔV3, because it does not describe inserting Gly-Ala-Gly into the deleted amino acids 297-329.

Applicants argue it is Dr. Srinivasan's opinion that those of skill in the art at the time of filing would have appreciated that the vv-ΔV3 mutant with the Δ297-329 deletion described in the specification included an insertion of Gly-Ala-Gly into the Δ297-329 deletion (pg 10, 1st full ¶). Applicants' arguments are not persuasive. Kmieciak (June 1, 1998) was not available at the time of filing (5-29-98). In no way does the specification teach, suggest or hint that Gly-Ala-Gly was inserted into the Δ297-329 deletion. One of skill would have had no way of knowing that the "Δ297-329 deletion" was the mutation described by Wyatt and that the mutation also included inserting Gly-Ala-Gly into the Δ297-329 deletion. Without such description, the specification does not adequately describe the structure of the vv-ΔV3, because it does not describe inserting Gly-Ala-Gly into the deleted amino acids 297-329. Therefore, the conclusion by Dr. Srinivasan is flawed because it is not based on any scientific or logical reasoning or on the specification as originally filed. As such, the specification does not provide adequate written description for the vv-ΔV3 vector.

The specification does not provide adequate written description for 1ΔV3, 7ΔV3 and 8ΔV3 mutants. The specification cannot provide adequate written description for 1ΔV3, 7ΔV3 and 8ΔV3 mutants because they were made from vv-ΔV3, which lacks written description for reasons above. The specification does not teach how the mutations were made, how the mutants differ from each other, how the mutants differ

from vv-ΔV3 or the structural elements of the mutants. It cannot be determined from the specification as originally filed what deletions were made in each of the 1ΔV3, 7ΔV3 and 8ΔV3 mutants. Therefore, the specification as originally filed does not provide adequate written description for the 1ΔV3, 7ΔV3 and 8ΔV3 mutants.

Applicants argue the specification provides written description for 1ΔV3, 7ΔV3 and 8ΔV3 mutants. Applicants summarize the method used to make 1ΔV3, 7ΔV3 and 8ΔV3 provided in ¶ 23 of the declaration by Dr. Srinivasan and on pg 9-10 of the response filed 8-12-04. Applicants' arguments are not persuasive. The methods in the declaration in ¶ 23 were not provided in the specification as originally filed.

In conclusion, the claims remain rejected under written description because the specification does not provide written description for one of skill to determine the structure of the only vectors mentioned in the specification having a deletion of the V3 loop as claimed, i.e. the vv-ΔV3, 1ΔV3, 7ΔV3 and 8ΔV3 vectors.

Claims 14, 15, 19, 28 and 32-36 remain rejected under written description because the specification does not adequately describe how to use the vectors or methods to vaccinate against HIV such that a therapeutic or prophylactic effect is obtained. Claims 14 and 15 are directed toward a method of making a vaccine against HIV. Claim 19 is directed toward a method of making a vaccine that induces cellular immunity against HIV. Claim 28 is directed towards a method of stimulating a CTL response against HIV. Claims 32-36 are directed towards a method of stimulating a CTL response in a patient. The only disclosed purpose for vaccinating against HIV,

inducing cellular immunity against HIV or stimulating a CTL response against HIV is to treat or prevent HIV infection (pg 1, line 12; pg 23, line 9). Therefore, vaccinating against HIV, inducing cellular immunity against HIV or stimulating a CTL response against HIV as claimed is only used to treat or prevent HIV infection.

The specification does not provide adequate written description for using any DNA encoding an envelope glycoprotein of HIV with a deletion in V3 capable of treating or preventing HIV, specifically capable of inducing a cellular immune response against HIV that is therapeutic or prophylactic. The specification does not teach obtaining a cellular immune response that is directed toward HIV or obtaining a therapeutic or prophylactic effect against HIV using the DNA or cells as claimed. The art at the time of filing did not teach how to obtain such an effect using DNA encoding an HIV envelope protein having a deletion in the V 3 loop. Without such guidance, the specification does not provide adequate written description for the structure of any DNA encoding an envelope glycoprotein of HIV with a deletion in V3 having the function of treating or preventing HIV.

Applicants argue that it is Dr. Srinivasan's opinion that the specification provides adequate description of how to make and use DNA as claimed as a vaccine against HIV, induce cellular immunity against HIV, and stimulate CTL activity as specified in those claims (¶ bridging pg 10-11 of response filed 8-12-04). See also ¶ 26 of the declaration by Dr. Srinivasan. Applicants' argument is not persuasive. The conclusion by Dr. Srinivasan is in error because it is not based on any scientific or logical reasoning or on the specification as originally filed. The conclusion is also in error because it

ignores the state of the art at the time of filing, which was that the art did not teach how to vaccinate against HIV using DNA encoding an HIV envelope protein having a deletion in the V 3 loop to obtain a therapeutic or prophylactic effect. Applicants have not provided guidance to overcome the state of the art. Applicants have not provided evidence that the examiner's description of the state of the art at the time of filing is in error. Applicants have not provided pre- or post-filing evidence indicating the teachings in the specification as originally filed were adequate to treat or prevent HIV. Applicants do not provide adequate guidance to make vv-ΔV3, 1ΔV3, 7ΔV3 or 8ΔV3 (see paragraphs above). Therefore, the specification as originally filed did not provide adequate written description for methods of making or using vectors for treating or preventing HIV.

II. Claims 14, 15, 19 and 21-36 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record.

The claims require DNA encoding an envelope glycoprotein of HIV having a deletion of the third variable loop. The specification discloses the WTP-2, WTP-5 and WTP-8 (pg 35, line 3; pg 36, line 16; Fig. 1) but does not teach they have a deletion of the V3 loop as claimed or provide the structure of the vectors. The only DNA disclosed in the specification having a deletion of the V3 loop as claimed are vv-ΔV3 (pg 26), 1ΔV3, 7ΔV3 and 8ΔV3 (pg 34). The specification does not enable one of skill to make

DNA encoding an envelope glycoprotein of HIV with a deletion of the V3 loop as claimed because the specification does not enable one of skill to make the vv-ΔV3, 1ΔV3, 7ΔV3 or 8ΔV3 vectors mentioned in the specification.

The specification does not enable one of skill to make vv-ΔV3. Kmieciak (June 1, 1998, J. Immunol., Vol. 160, pg 5676-5683) teaches vv-ΔV3 was made using "the Δ297-329 deletion" taught by Wyatt (Dec. 1992, J. Virology, Vol. 66, pg 6997-7004). The Δ297-329 deletion of Wyatt was a deletion spanning amino acids 297-329 of the V3 loop and an insertion of Gly-Ala-Gly in place of the loop. The specification does not teach, suggest or hint that Gly-Ala-Gly was inserted into the Δ297-329 deletion as taught by Kmieciak in view of Wyatt. Nor was Kmieciak available to one of skill at the time the application was filed (5-29-98). One of skill would have had no way of knowing that the "Δ297-329 deletion" described in the specification was the mutation described by Wyatt and that the mutation also included inserting Gly-Ala-Gly into the Δ297-329 deletion. Without such guidance, the specification does not adequately teach one of skill how to make vv-ΔV3 or the structure of the vv-ΔV3, because it does not describe inserting Gly-Ala-Gly into the deleted amino acids 297-329.

The specification does not enable one of skill to make 1ΔV3, 7ΔV3 and 8ΔV3 mutants. The specification cannot enable making 1ΔV3, 7ΔV3 and 8ΔV3 mutants because they were made from vv-ΔV3, which was not enabled for reasons above. The specification does not teach how the mutations were made, how the mutants differ from each other, how the mutants differ from vv-ΔV3 or the structural elements of the mutants. It cannot be determined from the specification as originally filed what deletions

were made in each of the 1ΔV3, 7ΔV3 and 8ΔV3 mutants. Therefore, the specification as originally filed does not enable making the 1ΔV3, 7ΔV3 and 8ΔV3 mutants.

Applicants argue it is Dr. Srinivasan's opinion that those of skill in the art at the time of filing would have appreciated how to make the nucleic acids and cells in claims 14, 15, 19 and 21-36 (pg 12, 1st full ¶). Applicants' arguments are not persuasive. Kmieciak (June 1, 1998) was not available at the time of filing (5-29-98). In no way does the specification teach, suggest or hint that Gly-Ala-Gly was inserted into the Δ297-329 deletion. One of skill would have had no way of knowing that the "Δ297-329 deletion" was the mutation described by Wyatt and that the mutation also included inserting Gly-Ala-Gly into the Δ297-329 deletion. Without such description, the specification does not enable one of skill to determine the structure of the vv-ΔV3, because it does not describe inserting Gly-Ala-Gly into the deleted amino acids 297-329. Therefore, the conclusion by Dr. Srinivasan is flawed because it is not based on any scientific or logical reasoning or on the specification as originally filed. As such, the specification does not enable one of skill to make the vv-ΔV3 vector.

Claims 14, 15, 19, 28 and 32-36 remain rejected under enablement because the specification does not adequately describe how to use the vectors or methods to vaccinate against HIV such that a therapeutic or prophylactic effect is obtained.

Claims 14 and 15 are directed toward a method of making a vaccine against HIV. Claim 19 is directed toward a method of making a vaccine that induces cellular immunity against HIV. Claim 28 is directed towards a method of stimulating a CTL

response against HIV. Claims 32-36 are directed towards a method of stimulating a CTL response in a patient. The only disclosed purpose for vaccinating against HIV, inducing cellular immunity against HIV or stimulating a CTL response against HIV is to treat or prevent HIV infection (pg 1, line 12; pg 23, line 9). Therefore, vaccinating against HIV, inducing cellular immunity against HIV or stimulating a CTL response against HIV as claimed is only used to treat or prevent HIV infection.

At the time of filing, it was unpredictable whether a nucleic acid construct would have a therapeutic or prophylactic effect against HIV. Ross of record (1996, Human Gene Therapy, Vol. 7, pg 1781-1790) states a major technical impediment to gene transfer is the lack of ideal gene delivery systems including vectors, promoters and modes of delivery (page 1782, col. 2, 1st full ¶). These technical parameters are required to obtain efficient delivery and sustained expression of the gene (Verma of record, Sept. 18, 1997, Nature, Vol. 389, pg 239-242; pg 239, 3rd col., line 10). The difficulties in sustaining expression of a gene cause unpredictability in obtaining a therapeutic or prophylactic effect in a patient (Ross, pg 1789, col. 1, 1st ¶). Therefore, the parameters required to obtain a therapeutic effect using DNA were unpredictable at the time of filing.

Regarding vaccines, it was unpredictable how to obtain a therapeutic effect against a virus using a single antigenic stimulus as a vaccine. Haynes of record (1993, Science, Vol. 260, pg 1279-1286) taught the classic approach to vaccine development involves exposing cells of the immune system to the proper antigenic stimulus, which stimulates a beneficial immune response. The prior art presents few examples where a

single antigenic stimulus, such as a small limited peptide or a whole protein is found to engender a therapeutic or protective immune response. The successful art-recognized immunogens used as vaccines are derived from whole killed or live attenuated pathogens, comprised of complex antigenic mixtures or comprised of inactivated toxins. Many of these successes were achieved with a certain degree of luck, influenced by some particular peculiarity or aspect of a given pathogenic agent. Therefore, it was unpredictable how to obtain a therapeutic effect against a virus using a single antigen.

Specifically regarding HIV vaccines, Stricker of record (Medical Hypotheses, June 1997, Vol. 48, pg 527-9; pg 527, last ¶ through all of pg 528) teaches that attempts to develop a vaccine against HIV have been unsuccessful. In fact, HIV infection has defied the creation of an effective vaccine or immunotherapeutic. Overall, a lack of understanding about cellular immunity against HIV, the sequence variability of HIV and the rapid replication of HIV, as disclosed by Bangham of record contribute the ineffectiveness of vaccines against HIV (Nov. 29, 1997, Lancet, Vol. 350, pg 1617-1621; pg 1617, top of col. 1). It is not known what renders an antigen capable of stimulating beneficial or protective CTL responses to HIV. Therefore, the art at the time of filing did not teach that the envelope glycoprotein of HIV could be used to induce a therapeutic cellular immune response against HIV. Thus, the parameters required to obtain a therapeutic cellular immune response against HIV was unpredictable at the time of filing.

The specification provides CTL and antibody-dependent cell-mediated cytotoxicity data *in vitro* (page 35-38), but does not provide any examples of inducing

cellular immunity against HIV *in vivo*. Nor does the specification provide adequate correlative evidence between *in vitro* data and *in vivo* results such that a therapeutic cellular immune response against HIV could be obtained *in vivo*.

The state of the art at the time of filing was that CTL assays *in vitro* produce variable results depending on the target cells used, the effector to target ratio used, and the incubation time (Lancki of record, 1992, Biotherapy, Vol. 5, pages 71-81; see page 72, column 1, line 1) CTL assays combine PBL and target cells that are artificially "loaded" with antigen. The amount of antigen required on the target cell surface to induce a CTL response depends upon the immunostimulatory epitope of the antigen, the type of immune response and the strength of the immune response desired. Moreover, CTL assays do not account for the complex interaction of the immune response and cytokine regulation that occurs *in vivo*. For example, Bachmann of record reviews the use of the cellular immune response both *in vivo* and *in vitro* in viral assay systems (1994, Current Op. Immunol. Vol. 6, pages 320-326). A comparison of sensitivities shows that radioactive CTL assays are more sensitive than *in vivo* assays, but that results of secondary *in vitro* stimulation need to be verified by *in vivo* assay. On page 323, Bachmann states one should be very cautious not to 'over-interpret' results obtained by a cytolytic assay where cells are stimulated *in vitro* because the results may be biologically irrelevant without *in vivo* confirmation. Therefore, it was unpredictable at the time of filing whether a CTL response obtained *in vitro* could be obtained *in vivo* or that a cellular immune response obtained *in vivo* equivalent to the cellular immune response obtained *in vitro* will have any biological relevance.

The *in vitro* CTL and ADCC assays disclosed in the instant application require PBMC isolated from an HIV patient and autologous B-LCL or Jurkat cells transfected with the vectors of the invention as target cells which do not correlate to cells or nucleic acids used to treat viral infection *in vivo*. The specification does not teach the strain of HIV in the patients used to make the PBMC *in vitro*, the level of antigen expression on the surface of target cells *in vitro*, the level of expression required *in vivo*, or how the immune response obtained *in vitro* correlates to response expected *in vivo*. It is not clear that the ratios of target to effector ratio used *in vitro* correlates to the ratio of transfected cells to effector cells that would occur *in vivo*. It addition, applicants activated the PBMC with antibodies, which is an artificial means used to increase the activity of the cytotoxic cells and does not correlate to conditions found in the HIV patients because patients PBMCs are not stimulated with anti-CD3 antibodies. In addition, the specification does not teach that the level of cellular immunity *in vitro* would have any therapeutic benefit in a patient. Given the state of the art regarding the lack of correlation between *in vitro* and *in vivo* cytotoxicity taken with the guidance provided in the specification, it would have required one of skill undue experimentation to determine the parameters required to obtain an cellular immune response *in vivo* that has a therapeutic or prophylactic effect.

Overall, the specification does not enable one of skill to use any DNA encoding an envelope glycoprotein of HIV with a deletion in V3 capable of treating or preventing HIV, specifically capable of inducing a cellular immune response against HIV that is therapeutic or prophylactic. The specification does not teach obtaining a cellular

immune response that is directed toward HIV or obtaining a therapeutic or prophylactic effect against HIV using the DNA or cells as claimed. The art at the time of filing did not teach how to obtain such an effect using DNA encoding an HIV envelope protein having a deletion in the V 3 loop. The specification does not teach any means of overcoming the unpredictability known in the art regarding how to use DNA to induce a cellular immune response or any immune response against HIV that is therapeutic or prophylactic. Without such guidance, the specification does not enable one of skill to use DNA encoding an envelope glycoprotein of HIV with a deletion in V3 as claimed to treat or prevent HIV.

Applicants argue it is Dr. Srinivasan's opinion that those of skill in the art at the time of filing would have appreciated how to use the nucleic acids and cells in claims 14, 15, 19 and 21-36 to treat or prevent HIV infection (pg 12, 1st full ¶). Applicants' arguments are not persuasive because Dr. Srinavasan's opinion is not based on any scientific or logical reasoning, on the specification as originally filed or on the art at the time of filing.

Applicants argue Rowland-Jones (1999) provides post-filing evidence demonstrating the methods and procedures described in the specification were adequate to make and use products capable of treating or preventing HIV. Specifically, applicants argue Rowland-Jones taught HIV-specific CTL was an important goal in controlling viral levels during infection. Applicants argue Kiska (2002) supports ΔV3 mutants that produce a CTL response (pg 12-13 of response filed 8-12-04). Applicants' arguments are not persuasive. Rowland-Jones, Kiszka and Kmieciak were not

available to one of skill in the art at the time of filing and do not teach treating or preventing HIV infection. Rowland-Jones, Kiszka and Kmieciak do not correlate to the invention originally disclosed in the instant application because they used different vectors. Applicants do not correlate the teachings in the specification as originally filed to the teachings of Rowland-Jones, Kiszka or Kmieciak. It is not readily apparent that the ΔV3 mutants described by Kiszka (pg 4223, col. 2, 1st full para.) correlate to the ΔV3 mutants described in the specification. The means by which ΔV3 mutants described by Kiszka induced a CTL response against gp160 *in vivo* is not described in the specification.

III. Claims 28-36 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

Claims 28-36 remain indefinite because the phrase "introducing into a vector DNA or liposome a nucleic acid encoding an envelope..." is grammatically unclear. The phrase "into a vector DNA or liposome" should be after the phrase "a nucleic acid... ...(V3)" to be grammatically correct. Furthermore, a "nucleic acid" as claimed does not encode anything because it a molecule; a nucleic acid sequence encodes an envelope protein. Finally, use of the phrase "vector DNA" is unclear because it does not have an art established meaning and cannot be found in the specification.

Applicants argue the claims specify that the nucleic acid encoding an envelope protein of HIV that comprises a deletion of the third variable loop is introduced into a

vector DNA or a liposome because the meaning of "introducing" and "vector" are described. Applicants' argument is not persuasive. Applicants have not addressed the fact that one nucleic acid does not encode any protein. It is not readily apparent that "vector" defined on pg 9, lines 20-21, is equivalent to "vector DNA" as claimed. applicants have not addressed the grammar of the phrase.

Claims 29 and 33 remain indefinite because it is unclear whether the "adjuvant" in claim 29 is the adjuvant of claim 28 or a different adjuvant. It is unclear if the phrase "mixing said vector DNA or liposome with a suitable adjuvant" in claim 29 is further limiting what the nucleic acid is introduced into in step a) of claim 28, whether the phrase is limiting what the is being mixed in step b) of claim 28, or whether the phrase is attempting to add a step to those in claim 28.

Applicants' statement that "if the claims do not specify the identity of the adjuvant, then the adjuvant recited in claim 29 may be the same or different from the adjuvant recited in claim 28" is noted but does not address the basis of the rejection. As written, it is unclear what the phrase is limiting.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

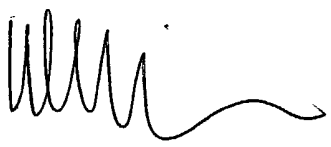
Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson



MICHAEL WILSON
PRIMARY EXAMINER